

REMARKS

Claims 1, 3-5, 9-10, 12-13, and 15-22 are pending in the instant application. Claims 1, 3-5, 9-10, 12 and 15-20 are amended. Claim 1 is amended to incorporate the subject matter of claims 8 and 14. Claims 4, 5, 9, 10, 12, and 15-16 are amended to depend from claim 1. Claims 3-5, 10, 17-19 and 20 are amended to recite proper antecedent basis from amended claim 1. Claims 2, 6-8, 11 and 14 are canceled. New claims 21 and 22 are added. Support for new claims 21 and 22 is found on page 12 at lines 1-12 in the specification as filed.

The description of Figure 5 in the specification is amended to better explain the figure according to the Examiner's suggestions.

I. Issues under 35 USC §102

Claims 1, 11, 14 and 17 are rejected under 35 U.S.C. § 102(b) as being anticipated by Qiagen® (1999a) as evidenced by Qiagen® (1999b). Applicants respectfully traverse.

Independent claim 1 is drawn to a method for separating and purifying a nucleic acid having a predetermined length from a nucleic acid sample solution. The method includes the step of selecting a rate of surface saponification and pore size of a solid phase, the solid phase being a porous film of a surface-saponified acetylcellulose. The method further includes adsorbing the nucleic acid of predetermined length to the solid phase, and then washing and desorbing the nucleic acid from the solid phase, thereby separating and purifying the nucleic acid of a predetermined length from the nucleic acid sample solution.

In contrast, the Qiagen® (1999a) reference discloses a method for separating nucleic acids of different lengths from a nucleic acid mixture by binding the nucleic acid molecules to a resin comprising an organic macromolecule having hydroxyl groups. The nucleic acid is washed to remove contaminants and then eluted with a high salt buffer.

Independent claim 1, alternatively, is drawn to a method for separating and purifying a nucleic acid from a mixture of nucleic acids by selecting a rate of saponification and pore size of a surface-saponified acetylcellulose porous film and then adsorbing the nucleic acid to the film. In contrast, the Qiagen® (1999a) reference does not disclose these elements

In order for the claims to be anticipated, each and every element of the claims must be

inherently or expressly disclosed in a single reference. Because the Qiagen® (1999a) reference does not disclose the element of selecting a saponification rate and pore size of a surface-saponified acetylcellulose porous film, the ‘Qiagen® (1999a) reference does not anticipate independent claim 1. Because claim 17 depends from claim 1, and therefore, incorporates the novel features of claim 1, claim 17 is allowable, at least by virtue of dependency. Claims 11 and 14 are canceled. Accordingly, Applicants respectfully request that the 102(b) rejection of claims 1, 11, 14 and 17 be reconsidered and withdrawn.

II. Issues under 35 USC §103(a)

US Patent No. 5,187,083 in view of US Patent No. 6,056,877

The Examiner has rejected claims 1, 11, 14 and 16-18 as obvious over US Patent No. 5,187,083 to Mullis (‘083) in view of US Patent No. 6,056,877 to Gjerde *et al.* (‘877). Applicants respectfully traverse.

As described above, independent claim 1 is drawn to a method for separating and purifying a nucleic acid from a nucleic acid sample solution by selecting a rate of surface saponification and pore size for a solid phase of a surface-saponified acetylcellulose porous film. The nucleic acid is then adsorbed, washed, and desorbed from the film.

In contrast, the ‘083 reference teaches a method for obtaining substantially pure DNA from blood cells by gently lysing cell membranes with a detergent to release a lysate containing high molecular weight DNA; allowing the lysate to stand for a period of time, and then filtering the lysate through a cellulose acetate filter to selectively trap high molecular weight DNA.

The ‘083 reference fails to teach or suggest the claim element of “selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose.” Likewise, the ‘877 reference does not teach or suggest this element.

In order for the claims to be obvious, each and every element of the claims must be disclosed or suggested in the combined references. Because the combination of the ‘083 reference and the ‘877 reference does not teach or suggest the step of separating and purifying a nucleic acid by “selecting a rate of surface saponification and pore size of a solid phase, said

solid phase being a porous film of a surface-saponified acetylcellulose”, each and every element of claim 1 is not disclosed or suggested in the combined references. Therefore, claim 1 is not obvious over the ‘083 reference in view of the ‘877 reference. Because claims 16-18 incorporate the features of claim 1, these claims also are not obvious over the combination of the ‘083 and the ‘877 reference. Claims 11 and 14 are canceled. Accordingly, Applicants respectfully request that the rejection of claims 1, 11, 14 and 16-18 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

EP 0512767 in view of US Patent No. 6,056,877

The Examiner has rejected claims 1, 11, 12 and 14-16 as obvious over EP 0512767 to Becton Dickinson & Company (EP ‘767) in view of the ‘877 reference. Applicants respectfully traverse.

As described above, independent claim 1 is drawn to a method for separating and purifying a nucleic acid from a nucleic acid sample solution by selecting a rate of surface saponification and pore size for a solid phase of a surface-saponified acetylcellulose porous film. The nucleic acid is then adsorbed, washed, and desorbed from the film.

The EP ‘767 reference fails to teach or suggest the claim element of “selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose.” Likewise, the ‘877 reference does not teach or suggest this element.

In order for the claims to be obvious, each and every element of the claims must be disclosed or suggested in the combined references. Because the combination of the EP ‘767 reference and the ‘877 reference does not teach or suggest the step of separating and purifying a nucleic acid by “selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose”, each and every element of claim 1 is not disclosed or suggested in the combined references. Therefore, claim 1 is not obvious over the EP ‘767 reference in view of the ‘877 reference. Because claims 15-18 incorporate the features of claim 1, these claims also are not obvious over the combination of the EP ‘767 reference and the ‘877 reference. Claims 11-12 and 14 are canceled. Accordingly,

Applicants respectfully request that the rejection of claims 1, 11, 12 and 14-18 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

EP 0512767 in view of US Patent No. 4,118,336

The Examiner has rejected claims 1-6, 10-12 and 14-18 as obvious over the EP '767 reference in view of US Patent No. 4,118,336 to Morishita *et al.* ('336). Applicants respectfully traverse.

In order for the claims to be obvious, each and every element of the claims must be disclosed or suggested in the combined references. As described above, the EP '767 reference does not teach or suggest the element of "selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose." Likewise, the '336 reference does not teach or suggest this feature. Because each and every element of claim 1 is not disclosed or suggested in the combined references, claim 1 is not obvious over the EP '767 reference in view of the '336 reference. Because claims 3-6, 10, 12 and 15-18 incorporate the features of claim 1, these claims also are not obvious over the combination of the EP '767 and the '336 reference. Claims 2, 11 and 14 are canceled. Accordingly, Applicants respectfully request that rejection of claims 1-6, 10-12 and 14-18 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

EP '767 in view of '877 and further in view of US Patent No. 5,695,946

The Examiner has rejected claim 13 as obvious over the EP '767 reference in view of the '877 reference and further in view of US Patent No. 5,695,946 Benjamin *et al.* ('946). Applicants respectfully traverse.

In order for the claims to be obvious, each and every element of the claims must be disclosed or suggested in the combined references. As described above, the EP '767 reference does not teach or suggest the element of "selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose." Likewise, neither the '336 reference nor the '946 reference teach or suggest this feature. Because claim 13 incorporates the features of claim 1, each and every element of claim 13 is not

disclosed or suggested in the combined references. Therefore, claim 13 is not obvious over the EP '767 reference in view of the '877 reference and further in view of the '946 reference. Accordingly, Applicants respectfully request that the rejection of claim 13 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

EP '767 in view of '336 and '877 and further in view of '946

The Examiner has rejected claim 13 as obvious over the EP '767 reference in view of the '336 reference and the '877 reference and further in view of the '946 reference. Applicants respectfully traverse.

In order for the claims to be obvious, each and every element of the claims must be disclosed or suggested in the combined references. As described above, the EP '767 reference does not teach or suggest the element of "selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose." Likewise, neither the '336 reference, the '877 reference, nor the '946 reference, teach or suggest this feature. Because claim 13 incorporates the features of claim 1, each and every element of claim 13 is not disclosed or suggested in the combined references. Therefore, claim 13 is not obvious over the EP '767 reference in view of the '877 reference and the '336 reference, and in further view of the '946 reference. Accordingly, Applicants respectfully request that the rejection of claim 13 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

EP '767 in view of '877 and further in view of WO 99/13976

The Examiner has rejected claims 19 and 20 as obvious over the EP '767 reference in view of the '877 reference and further in view of the WO 99/13976 reference. Applicants respectfully traverse.

In order for the claims to be obvious, each and every element of the claims must be disclosed or suggested in the combined references. As described above, the EP '767 reference does not teach or suggest the element of "selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose." Likewise, neither the '877 reference nor the WO 99/13976 reference teach or suggest this

feature. Because claims 19 and 20 incorporate the features of claim 1, each and every element of claims 19 and 20 are not disclosed or suggested in the combined references. Therefore, claims 19 and 20 are not obvious over the EP '767 reference in view of the '877 reference, and further in view of the WO 99/13976 reference. Accordingly, Applicants respectfully request that the rejection of claims 19-20 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

EP '767 in view of '336, '877 and further in view of WO 99/13976

The Examiner has rejected claims 19 and 20 as obvious over the EP '767 reference in view of the '336 reference and the '877 reference and in further view of the WO 99/13976 reference. Applicants respectfully traverse.

In order for the claims to be obvious, each and every element of the claims must be disclosed or suggested in the combined references. As described above, the EP '767 reference does not teach or suggest the element of "selecting a rate of surface saponification and pore size of a solid phase, said solid phase being a porous film of a surface-saponified acetylcellulose." Likewise, neither the '336 reference, the '877 reference, nor the WO 99/13976 reference, teach or suggest this feature. Because claims 19 and 20 incorporate the features of claim 1, each and every element of claims 19 and 20 are not disclosed or suggested in the combined references. Therefore, claims 19 and 20 are not obvious over the EP '767 reference in view of the '336 reference and the '877 reference, and in further view of the WO 99/13976 reference. Accordingly, Applicants respectfully request that the rejection of claims 19-20 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

III. Issues under 35 USC §112, first paragraph

Claims 1-20

Claims 1-20 are rejected under 35 USC § 112, first paragraph, because the claims contain subject matter that would not enable a skilled artisan to make and use the invention commensurate with the claims. Applicants respectfully traverse.

The Examiner asserts that although the specification enables the separation of a 1.3 kb fragment from a 48 kb DNA fragment, the specification does not reasonably provide enablement

for the separation of any sized nucleic acid fragments from within a mixture containing any number and type of nucleic acid fragments of different lengths using any organic macromolecule.

Applicants respectfully disagree with the Examiner's assertion. First of all, the Examiner mischaracterizes the breadth of the claims. The present claims are drawn to separating nucleic acids using a porous film of a surface-saponified acetylcellulose. Thus, the present claims are not drawn to "any organic macromolecule", (see, Office Action at page 6), but rather to separations employing a surface-saponified acetylcellulose.

Second, Applicants respectfully disagree that the present specification is not enabled for the separation of "of any sized nucleic acid fragments." (See, Office Action at page 6). Applicants contend that the instant specification teaches a skilled artisan how to separate a wide size range of nucleic acid fragments. For example, guidance is provided in Example 1 (page 26 in the specification as filed), which describes the separation of a 1.3 kb nucleic acid fragment or a 48 kb fragment from a nucleic acid mixture. Thus, the specification teaches a skilled artisan how to separate both low molecular fragments and high molecular weight fragments. Moreover, attached is a Declaration under 37 C.F.R. § 1.132 by Inventor Toshihiro Mori, which demonstrates the separation of a 200 bp fragment and a 1,500 bp fragment. These fragments were separated according to the guidance provided in Example 1. Thus, the Mori Declaration provides embodiments, in addition to those specifically described in the working examples, further supporting Applicants' contention that the scope of the claims is supported by the guidance in the specification. The Examiner should note that altogether, there is evidence for separations according to the invention over three orders of magnitude of size range.

The specification also describes how to separate and purify nucleic acids of a variety of predetermined lengths from a nucleic acid mixture that contains nucleic acid fragments of different lengths. For example, the specification describes how to separate a short nucleic acid fragment from a nucleic acid mixture. On page 12 at lines 4-14 the specification states "by using a porous membrane having a low surface-saponification rate...in combination with a porous membrane having a high surface-saponification rate (e.g. higher than 50% of surface-saponification rate, e.g., 100% of surface saponification rate), there is provided a method for

separating and purifying a relatively short (e.g., 10 kb or shorter, more preferably 2 kb or shorter) nucleic acid from the nucleic acid mixture which contains nucleic acids having different lengths.” Moreover, the specification teaches the artisan that ‘by preparing a plurality of porous membranes within a range of surface saponification rates and a plurality of porous membranes, having a range of pore sizes, a nucleic acid can be separated and purified.’ (See, page 10 at lines 21-30). Therefore, the specification teaches the skilled artisan how to separate a nucleic acid of a particular length from any particular mixture that contains nucleic acid fragments of different lengths.

The Examiner, however, asserts that such disclosure is insufficient, in part, because the art is unpredictable. In support of his assertion, the Examiner cites references, which state, *inter alia*, that cellulose acetate membranes will not bind to DNA, that certain DNA molecules bind tightly to cellulose and that the binding energy of RNA to cellulose esters can be low. Applicants contend, however, that these references are not persuasive indicators of the level of predictability of the art. Because these references do not discuss the level of predictability of the art as related to the instant invention, *i.e.* the ability of nucleic acids to bind to a surface saponified acetylcellulose, the Examiner fails to provide “acceptable evidence or reasoning which is inconsistent” with the specification, and therefore has not met the initial burden of showing nonenablement. *In re Marzocchi*, 439 F. 2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). Moreover, a mere assertion of unpredictability cannot establish *prima facie* lack of enablement in the face of evidence of a broad scope of operability of the invention as is shown here by the working examples and the Mori Declaration.

Thus, Applicants contend that the specification provides adequate disclosure to enable a person of skill in the art to make and use the invention commensurate with the claim scope. Accordingly, Applicants respectfully request that the 112, first paragraph, rejection of claims 1-20 be reconsidered and withdrawn.

Claim 7

Claim 7 is rejected under 35 USC 112, first paragraph, as failing to comply with the enablement requirement. Claim 7 is canceled. Therefore, this rejection is moot.

IV. Issues under 35 USC §112, second paragraph

Claims 1-20 are rejected under 35 USC 112, second paragraph, as being indefinite.

Specifically, the Examiner asserts that claims 1-7 and 10-20 are indefinite in the recitation 'separating and purifying a nucleic acid having a predetermined length' in the preamble of the claim because the method steps to not correlated with the preamble.

Claim 1 has been amended to recite the steps of selecting a rate of saponification and pore size of a solid phase; adsorbing a nucleic acid of predetermined length from a nucleic acid solution; washing and desorbing the nucleic acid of predetermined length, thereby separating and purifying said nucleic acid of predetermined length from said nucleic acid sample solution. Thus, the method steps correlate with the preamble. Because a skilled artisan understands the scope of claim 1, this claim is not indefinite. Likewise, claims 3-5, 9-10, 12-13, and 15-20 also, appropriately, correlate method steps with the preamble as they depend from claim 1 which is not indefinite. Therefore, claims 3-5, 9-10, 12-13 and 15-20 are also not indefinite. Claims 2, 6-8, 11 and 14 are canceled. Accordingly, Applicants respectfully request that the 112, second paragraph, rejection of claims 1-20 be reconsidered and withdrawn.

Double Patenting*US Patent Application No. 10/305,110*

Claim 1 stands provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending US Patent Application No. 10/305,110 ('110). This rejection is provisional. Thus, until claims issue from the '110 application, no action is required on the part of Applicants. (See, M.P.E.P. § 804, I, A, 1).

US Patent Application No. 10/621,329

Claims 1-7 and 10-20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of copending US Patent Application No. 10/621,329 ('329). This rejection is provisional. Thus, until claims issue

from the '329 application, no action is required on the part of Applicants. (*See, M.P.E.P.* § 804, I, A, 1).

US Patent Application No. 10/621,412

Claims 1-7 and 10-20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of copending US Patent Application No. 10/621,412 ('412). This rejection is provisional. Thus, until claims issue from the '412 application, no action is required on the part of Applicants. (*See, M.P.E.P.* § 804, I, A, 1).

US Patent Application No. 10/208,336

Claims 1-7 and 10-20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of copending US Patent Application No. 10/208,336 ('336). This rejection is provisional. Thus, until claims issue from the '336 application, no action is required on the part of Applicants. (*See, M.P.E.P.* § 804, I, A, 1).

US Patent Application No. 10/808,411

Claims 1-7 and 10-20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-34 of copending US Patent Application No. 10/808,411 ('411). This rejection is provisional. Thus, until claims issue from the '411 application, no action is required on the part of Applicants. (*See, M.P.E.P.* § 804, I, A, 1).

US Patent Application No. 10/932,138

Claims 1-7 and 10-20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of copending US Patent Application No. 10/932,138 ('138). This rejection is provisional. Thus, until claims issue

from the '138 application, no action is required on the part of Applicants. (*See, M.P.E.P.* § 804, I, A, 1).

US Patent Application No. 10/975,469

Claims 1-7 and 10-20 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-35 of copending US Patent Application No. 10/975,469 ('469). This rejection is provisional. Thus, until claims issue from the '469 application, no action is required on the part of Applicants. (*See, M.P.E.P.* § 804, I, A, 1).

In view of the above, Applicants respectfully submit that the present claims are fully enabled. Reconsideration and withdrawal of the outstanding rejections are respectfully requested.

If the Examiner has any questions concerning this application, the Examiner is requested to contact Marc S. Weiner, Reg. No. 32,181 at the telephone number of (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: *May 22, 2006 (mon.)*

Respectfully submitted,

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Attachment: Declaration under 37 CFR 1.132 by Toshihiro Mori